Ex Vivo Expansion and In Vivo Self-Renewal of Human Muscle Stem Cells.

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Public Summary:
In this paper, the authors describe a method to isolate stem cells from tissue samples of adult human muscle. They use cell purification techniques to isolate the stem cells away from the other cells in the tissue, and they take advantage of sophisticated molecular analysis to come up with conditions that allow them to grow up these stem cells in culture, thus providing the methods to obtain many times the number of the original stem cells. This is essential for using stem cells for therapies for muscle injuries or muscle diseases. Toward that end, the authors demonstrate how effectively the stem cells are to make new muscle when transplanted back into a mouse that has a muscle injury.

Scientific Abstract:
Adult skeletal muscle stem cells, or satellite cells (SCs), regenerate functional muscle following transplantation into injured or diseased tissue. To gain insight into human SC (huSC) biology, we analyzed transcriptome dynamics by RNA sequencing of prospectively isolated quiescent and activated huSCs. This analysis indicated that huSCs differentiate and lose proliferative potential when maintained in high-mitogen conditions ex vivo. Further analysis of gene expression revealed that p38 MAPK acts in a transcriptional network underlying huSC self-renewal. Activation of p38 signaling correlated with huSC differentiation, while inhibition of p38 reversibly prevented differentiation, enabling expansion of huSCs. When transplanted, expanded huSCs differentiated to generate chimeric muscle and engrafted as SCs in the sublaminar niche with a greater frequency than freshly isolated cells or cells cultured without p38 inhibition. These studies indicate characteristics of the huSC transcriptome that promote expansion ex vivo to allow enhanced functional engraftment of a defined population of self-renewing huSCs.